REMARKS

Entry of this amendment and favorable reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-99 are in this case. Claims 21-50 and 71-99 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-20 and 51-70 have been rejected. Claims 1 and 51 have now been amended.

Response to Examiner's comments

The Examiner states that the phrase "medium flow conditions" is not clear. Specifically, the Examiner states that it is not clear whether medium refers to the flow conditions, or to the medium flowing through the bioreactor.

Claim 1 and 51 have now been amended to better and more clearly define the culturing conditions for growing the stromal cells. These claims no longer recite the phrase "medium flow conditions thus rendering moot Examiner's rejections with respect to the use of this phrase.

An example of conditions which can be used for medium flow is described in Page 33 lines 24-26 of the instant application.

The Examiner further states that step (b) of claim 1 and step (ii) of claim 51 are unclear as to when the cells are seeded in the bioreactor. Specifically, the Examiner is uncertain if the cells are seeded before, during or after culturing of stromal cells.

Claims 1 and 51 have now been amended to better define the method steps of the present invention.

Steps (a) and (b) of claim 1 now read:

> (a) culturing in a stationary phase plug-flow bioreactor a stromal cell culture under flow of a culture medium on a substrate in the form of a sheet, said substrate including a non-woven fibrous matrix forming a physiologically acceptable three-dimensional network of fibers to thereby generate a three dimensional

stromal cell culture; and

(b) seeding the undifferentiated hemopoietic stem cells or progenitor cells into said stationary phase plug-flow bioreactor ***including said three dimensional stromal cell culture***, thereby expanding/maintaining the undifferentiated hemopoietic stem cells or progenitor cells. (Emaphasis added).

Claim 51 recites similar limitations.

The Examiner finds the 37 CFR Declaration unpersuasive. Specifically, the Examiner states that the declaration fails to describe bioreactor structure and culture conditions to enable determining whether the 3 fold increase in stem cell growth under the conditions of the present invention as compared to the conditions described by Naughton is significant and whether the claims are commensurate in scope with the procedure used in the declaration according to the invention.

The Appendix attached herewith has been amended to include the missing technical data. The procedures used in the experiments presented in the declaration including bioreactor, substrate, flow and cells are similar to those described in the "Materials and Experimental Methods" section of the instant application [Pages 28-32 (e.g., Bioreactor structure Page 28 lines 19-28 and Page 29 lines 1-6] and as such are covered by the claimed methods of the present invention,. As such, it is Applicant strong opinion that the claims are commensurate in scope with the procedure used in the declaration according to the present invention.

The Examiner further states that Sussman et al. and Stephanopolous et al. suggest that using non-woven fiber sheets and continuous flow culturing will result in better cell growth.

The Examiner states that according to Sussman et al. the fiber sheet provides increased attachment surface and provides adequate porosity for entrance of cells and nutrients and for removal of wastes. Such conditions are expected to result in better cell growth.

The Examiner states that Stephnopoulos et al. disclose the advantages of

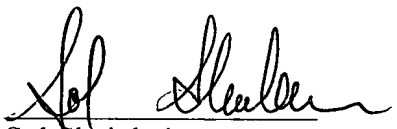
convective culture medium flow that would have been expected to result in better cell growth over when using static conditions.

Applicant notes that neither Sussman nor Stephanopoulos et al. suggested to use their ***combined*** teachings to grow undifferentiated cells or progenitor cells in the presence of highly dense cultures of stromal cells. Naughton et al., who attempted the growth of committed cells (Column 21 lines 21-28) on a three dimensional stromal cell culture did not use flow conditions and therefore could not achieve the inherently high stromal cell density which results from culturing under flow and which is required for growing non-differentiated stem cells or progenitor cells.

It is, therefore, the Applicant's strong opinion that these combined teachings fail to render claims 1-20 and 51-70 obvious.

In view of the above amendments and remarks, it is respectfully submitted that claims 1-20 and 51-70 are now in condition for allowance. An early Notice of Allowance is respectfully and earnestly solicited.

Respectfully submitted,



Sol Sheinbein
Registration No. 25,457

Date: March 23, 2004.

Enc.
Appendix
Declaration by Dr. Shai Meretski